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Neural Control of the Heart: Summary of Discussion

Moderator: **Henry D. McIntosh, MD, FACC;** *Panelists:* **Robert S. Eliot, MD, FACC, Lawrence E. Hinkle, Jr., MD, Lino Rossi, MD, James E. Skinner, MD, Borys Surawicz, MD, FACC, James V. Warren, MD, FACC**

Drs. Warren and Hinkle succinctly posed one of the questions foremost in the minds of most of the participants at this Conference. "Why do not all or at least most people with advanced coronary heart disease experience sudden cardiac death? Even more importantly, why do not many or even a few completely normal people experience sudden cardiac death?"

Dr. Warren specifically asked, "Why doesn't cardiac syncope occur in most individuals who have coronary artery disease when they engage in a heated argument or even when they become emotionally upset during the normal course of life?" He observed that "most people are remarkably durable. We live 60, 70 and frequently 80 years. The engine doesn't cough once. Cardiac syncope in the truly normal person is an exceedingly rare occurrence." He then asked, "What are the protective mechanisms that keep our hearts going despite the potential of all these 'nasty reflexes'?"

Dr. Hinkle brought into clear perspective a major challenge for future research by relating some of the observations made while following up for 5 to 10 years a group of 700 individuals thought to be representative of the general population. In that group, there were originally a significant number of subjects who had very frequent ventricular arrhythmias as well as short runs of tachycardia. There were indeed some who had as many as 10 runs of tachycardia a day, and most of these men were still alive 10 years later. "We estimate that many of these individuals might have had on the order of 30,000 or more such episodes, all of which were extinguished after a few beats. The death rate in patients in this group, who also had myocardial ischemia or previous myocardial hypertrophy, has only been about 6%. When death occurred, the individuals died with statistically unexpected frequency while they were awake or after activities or exercise. But the type of activity, walking or running for a train, walking up three flights of stairs or having an argument with a friend, was typical of what they had been doing day in and day out for many years.

"Now the question I have to ask," Dr. Hinkle continued, "is what mechanism was protecting these men as they went about their daily lives? What mechanisms are protecting all of us under similar circumstances? How can we recognize them? Because if we do, it seems to me, it will lead us to some very useful therapeutic information."

Dr. Skinner emphasized that sudden cardiac death was due to a number of different causative factors. The most important of these most certainly is coronary artery disease. "But that process alone doesn't invariably kill you. There are people who have very extensive coronary heart disease who are alive, so there must be something else that is necessary. These factors together, one known and one or more unknown, then constitute the necessary and sufficient causes for sudden cardiac death." Dr. Skinner then observed that, "In the laboratory animal, you can electrically stimulate the brain in a certain location. If the animal is reacting to psychological stressors in the environment, ventricular fibrillation will quickly result without coronary artery occlusion. In such a situation, ventricular fibrillation occurs much more quickly than when the coronary artery is occluded. Ventricular fibrillation after coronary artery occlusion in the experimental animal in the absence of the stimulation does not occur for 9 to 14 minutes." Dr. Warren accepted this observation and agreed that he is sure that it can happen . . . "Yet, common medical experience indicates that it doesn't happen!"

Dr. Eliot claimed that we have been partially paralyzed by terminology. "Sudden coronary death isn't sudden. There are many 'softening up' processes in the myocardium. Overtime, the coronary system develops fixed stenoses and becomes plagued by variable stenoses due to spasm. Although the electrical system's vulnerability can be altered by a variety of processes, none of these changes is likely to be sudden . . . the alterations develop slowly. Although the end result may be sudden, it is due to a myriad of things requiring time to metabolically and physiologically 'soften' the individual to the point that it makes a difference."

Dr. Surawicz stated that he believed that there was no evidence, despite what had been presented by the panel members, that stress had any relevance to cardiac arrest. His conclusion was based on reading the newspaper and

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watching television every day and seeing soldiers marching into battle, parachute jumpers, people on death row, people in the Three Mile Island community threatened by high level panic, people in earthquakes and people exposed to other extremely stressful situations, all panic situations affecting large groups of people, "and I have never read anything about anybody dying suddenly."

Such anecdotal observations, dramatically described by Dr. Surawicz, did not alter Dr. Skinner's conviction of the importance of stress. He again stated that sudden death "is a multifactorial event. Stress alone doesn't cause it, but there can be a unique combination of factors that produce the effects that have been described. It is this combination that produces the lethal event. It is no accident . . . it can be explained. There are underlying mechanisms that can now be identified. Clearly, a single factor is not sufficient explanation. Stress alone does not cause sudden cardiac death. You have to have coronary artery disease and you have to have some other factor or factors that as yet we have not identified."

The importance of several destructive factors was supported again by Dr. Eliot. In his judgment, stress was frequently an important factor. The importance of the effect of stress, according to Dr. Eliot, could be appreciated from the occurrence of coagulative myocytolysis in the myocardium. In his experience, such a lesion was present in the vast majority of victims of sudden cardiac death. This lesion was also present in the heart of patients dying with pheochromocytoma and could easily be produced in the experimental animal by administration of excessive exogenous catecholamines. These observations led him to conclude that it could serve as the "footprint of the softening up process" that might eventually facilitate the occurrence of sudden cardiac death. However, Dr. Rossi challenged the specificity of the lesion as a marker of catecholamine excess. He stated that the lesion described by Dr. Eliot was "commonplace in the dynamics of acute myocardial infarction, and cannot be considered, in my opinion, a hallmark of catecholamine sudden cardiac death."

Conclusions. The discussion that followed indicated that not only were there doubts that stress was of any major importance in the final common pathway leading to sudden cardiac death, but also there was doubt that we could confirm by pathologic examination of the heart the possibility that stress-induced catecholamine excess played a role in sudden cardiac death. The only area of almost unanimous agreement was that sudden death was multifactorial in cause, and one of the major factors, but not in itself sufficient cause for sudden death, was advanced coronary heart disease. Furthermore, there were undoubtedly protective mechanisms that were operative, and these protective mechanisms were probably neural in origin. "Otherwise, all of us would die," as Dr. Warren so dramatically put it, "from those 'nasty reflexes' involving the central nervous system." All agreed that we do not have the slightest idea of the nature of the protective mechanism or mechanisms, and therein lies the great challenge regarding future research related to sudden cardiac death.